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Dr. Jordan Gutterman
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Dear Jordan

I have nothing but gleeful approbation to offer for your essay on therapeutic research. I was particularly glad to have your own memoir on the development of interferon. I was in Burnet's lab at Melbourne when we first had word of Alick Isaacs' findings about it, in relation to viral interference in flu! So I am closer to that history than you might ever have thought.

Patient capital is very much the key. Everything in our tax and financial assessment systems goes against it! And of course the bridging of the most basic research with applicability is the hardest.

But capital also has to be wise. I'd guess there are 10,000 potential useful therapeutics to be gleaned from the 100,000 units of the human genome alone. At $10^8 each, their total development would be about a trillion dollars -- or the total of our health care expenditure for the foreseeable future. A prudent triage is inevitable, even for products that might be technical successes. The marketing of venture investments has to be made more authentic, and get better substantive advice. I've had little (but some) luck trying to convey that to Wall Street in this town.

I tried to introduce the ideas we now call combinatorial chemistry in 1956 (sic); and this met with no success at all for over 30 years! It just didn't fit the culture; nor could I get funding to pursue it. Well, you know what has happened now, but how many more fruits there might have been in the interval! Not to mention my own being passed over -- on that one; but who's to complain.

I love that quote from Voltaire; but you have it second hand. Can you corroborate it? "Doctors pour drugs of which they know little, to cure diseases of which they know less, into human beings of which they know nothing."

You were kind enough to cite some of my own writings; but perhaps you don't know them all, so enclosed are a few others pertinent to your discussion.

The mixed-sector institutions you mention are most urgently needed in the vaccine area. I don't think they will take the place of private enterprise capital in most of the market; but

they would have a role. You are bound to hear screams about unfair competition from existing industry, and from academics who want the best of both worlds (academic freedom and security; and get rich quick).

We could have some subtle discussion about what is meant by studying "patients". I am imbued with the mystique of the clinical research center; but truth be told, most of the investigation is not done ON patients, but in cells, tissues, fluid samples from them. Of course clinical insight and judgment, and a sharp nosological and epidemiological sense still have important functions. But most clinical investigation is also a cycle in which observation of the patient is the opening gambit, and the end game; and most of the action in between. Whether single individuals can continue to occupy all of those game positions is less obvious, though as a matter of creative challenge, I deplore the move to complex teams.

So much to say about FDA! Should every really new drug receive the privileges of an orphan? We probably badly need that in the antibiotic field. I couldn't agree with you more about the need to encourage research on combinations, especially in cancer and infections! And the FDA mentality encumbers that mightily. Still on FDA, I have long advocated the earlier release of drugs (for sale) to specially licensed prescribers who would be obligated to make a scientific study of side-effects. Most faults of drugs are not discoverable until they hit the larger market, so FDA's basic strategy is to let Europe and Asia provide the guinea pigs for a few years while the US makes up its mind. We need an objective, cost benefit study of the net consequences of that delay.

Yours sincerely,

Joshua Lederberg